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TOXICITY OF HIGH DENSITY JET FUEL COMPONENTS

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TECHNICAL REVIEW AND APPROVAL

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The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

Anthony A. Thomas

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Two constituents of a synthetic jet engine fuel were evaluated for toxicologic effects. These constituents of JP-9 fuel were perhydromethylcyclopentadiene (RJ-4) and bicycloheptadiene (RJ-5). Excess tumor lesions over control levels were seen in a small number of rats and mice held for a one year observation period following six months repeated daily inhalation exposures to RJ-5.

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PREFACE

This technical report of the Toxic Hazards Research Unit (THRU) concerns work performed by the Department of Community and Environmental Medicine of the University of California, Irvine on behalf of the United States Air Force under Contract Number F33615-76-C-5005.

The current contract for operation of the Laboratory was initiated in 1975 under Project 6302 "Occupational and Environmental Toxic Hazards in Air Force Operations," Task 01 "Toxicology of Propellants and Materials" Work Unit Number 63020115. K. C. Back, Ph.D., Chief of the Toxicology Branch was the technical contract monitor for the Aerospace Medical Research Laboratory.

Acknowledgement is made to Jose Diaz, William Steinhagen, and Gary Fogle for their significant contributions to this research project and for assistance in the preparation of this report. Acknowlegement is also made to Dr. Arthur Stein, Major Kenneth Ayres and Major Robert Amster for their assistance in the evaluation of pathologic specimens described in this report.

SECTION I

INTRODUCTION

A new fuel has been developed for extending the flight range of aircraft before refueling. The fuel designated JP-9 is a mixture of three primary ingredients, namely RJ-4, RJ-5, and methylcyclohexane. RJ-4 and RJ-5 are high density hydrocarbons yielding a greater BTU output per unit volume than conventional jet aircraft fuels. They also have a higher viscosity causing pumping or flow problems at low temperatures which is the reason for the addition of methylcyclohexane to the mixture. The precise composition of the JP-9 fuel is not fixed but will be tailored for use in specific aircraft systems. Although no toxicity data are available for JP-9 fuel, it is not meaningful to evaluate the entire mixture for two reasons: first, the actual mixture has not been set; and second, methylcyclohexane is extremely volatile in comparison with the other constituents and would dominate the vapor exposure mixture, thus masking the effects of RJ-4 and RJ-5.

Acute and chronic toxicity studies on methylcyclohexane have been reported by Treon et al. (1943). Acute exposures of rabbits to inhaled concentrations of methylcyclohexane above 10,000 ppm (≈40 mg/liter) caused significant weight loss, narcosis, and convulsions while a concentration of 15,227 ppm was fatal in slightly over one hour. Repeated daily, 5-hour exposures of rabbits to concentrations of 1162 ppm or lower for periods up to 10 weeks produced no measurable or observable signs of toxicity.

Some of the physical/chemical properties of RJ-4, RJ-5, and methylcyclohexane are shown in Table 1. RJ-4 is a mixture of isomers of perhydromethylcyclopentadiene. RJ-5, also known as "Shelldyne H", is a mixture of reduced dimers of bicycloheptadiene. Noticeable in Table 1 are the very low vapor pressures of RJ-4 and RJ-5 relative to that for methylcyclohexane. The vapor pressures of RJ-4 and RJ-5 are approximately 100 and 1500 times less, respectively, than methylcyclohexane. This information is basic to the consideration of that hazard (the probability of injury in use) of these fuels.

To examine the acute inhalation hazard and to obtain experimentally determined saturation concentrations as an aid in the selection of vapor levels for the chronic study, groups of six rats each were exposed for 6 hours to essentially saturated vapors of each compound. No adverse effects were seen during exposure. Pathologic examination after 14-day postexposure observation showed no abnormalities. Peroral doses of 4 g/kg RJ-5 in corn oil were not lethal to a group of 3 rats; however, 2 of 3 mice succumbed to a 250 mg/kg dose.

The toxicity of RJ-4 and RJ-5 has not been reported previously and it was, therefore, necessary to conduct chronic inhalation studies with these materials to evaluate their potential health hazard. Accordingly, concentrations of 0.15 mg/liter RJ-5 and 2 mg/liter RJ-4 were selected for a 6-month chronic exposure of 4 animal species. The levels chosen were slightly below saturation vapor pressures so that condensation on chamber surfaces would not occur.

SECTION II

EXPERIMENTAL ANIMALS, MATERIALS AND METHODS

Each experimental group and the unexposed chamber controls consisted initially of 4 female and 4 male beagle dogs, 50 male CFE rats, 40 female CF-1 mice, and an uneven mixture of male and female Macaca mulatta monkeys, 4 per chamber.

TABLE 1. PHYSICAL-CHEMICAL PROPERTIES OF RJ-4, RJ-5, AND METHYLCYCLOHEXANE

	RJ-4 T.H. Dimer	RJ-5	MCH
Empirical Formula	$C_{12}H_{20}$	$C_{14}H_{20}$	C_7H_{14}
Molecular Weight	164	188	98
Boiling Point (°F)	431	522	213
Vapor Pressure (70°F)	0.354 mmHg	0.025 mmHg	42 mmHg
Density (70°F)	0.925 g/ml	1.0813 g/ml	0.7660 g/ml

Groups of animals were housed in separate large chambers operated with nominal airflows of 40 cfm at a slightly reduced pressure, 725 mmHg, to avoid leakage of the chamber air into the laboratory. Temperatures were controlled at 72 ± 2 F and relative humidity at 50 ± 10%. Exposures were conducted on a 6 hour/day, 5 day/week schedule. No exposures were made on weekends and holidays. Upon completion of the daily exposures, the chambers containing RJ-4 and RJ-5 were purged with air for 30 minutes before lifting the chamber tops for cleaning and feeding of the animals.

Although expected to be low, the toxicities of the chemicals under study were unknown except for the minimal acute animal information mentioned earlier. Personnel working with these materials avoided skin contact and inhalation. The vapor generation apparatus and chemical supplies were located in ventilated hoods, and the areas were designated no smoking zones.

The chamber concentrations of RJ-4 and RJ-5 were continuously monitored using flame ionization hydrocarbon analyzers. The generation and monitoring techniques were identical to those used during exposures of animals to JP-4 jet fuel (MacEwen and Vernot, 1974).

To measure the chronic toxicity of RJ-4 and RJ-5, a limited number of parameters were selected, with the view toward increasing the variety of tests should the basic battery reveal trends or deleterious effects during the course of the study.

All exposed animals were observed for signs of toxic stress as well as mortality. Gross and histopathologic examinations were made on all dead animals. Body weights of dogs, monkeys and rats were measured on a biweekly schedule. Table 2 shows the reduced battery of clinical hematology and chemistry tests performed on blood samples taken from dogs and monkeys on a biweekly basis. Complete batteries of clinical laboratory tests were made at the start and at the completion of the exposures. These tests included, in addition to those shown in Table 2, creatinine, chlorides, cholesterol, BUN, total inorganic phosphorus, bilirubin, and serum triglycerides. These "banked" serum samples were stored until histopathology reports were received and reviewed. Twenty rats and mice from each of the study groups were retained for one year observation following exposure termination to evaluate any postexposure effects from RJ-4 and/or RJ-5 inhalation. All remaining animals were sacrificed at exposure termination and submitted for gross and histopathologic examination. Major organs were taken from 20 rats from each group and weighed for comparison of mean organ weights and organ to body weight ratios.

TABLE 2. CLINICAL BLOOD TESTS PERFORMED ON RJ-4, RJ-5 EXPOSED AND CONTROL DOGS AND MONKEYS

HCT	Total Protein
HGB	Calcium
RBC	Glucose
WBC	Alkaline Phosphatase
Sodium	SGPT
Potassium	Differential Cell Count
Albumin/Globulin	

SECTION III

EXPERIMENTAL RESULTS

A curious effect occurred in the rats exposed to RJ-4. Diarrhea was evident in the majority of the rats at 10 weeks of exposure and continued throughout the duration of the exposure portion

of the study. Frequent postexposure observation of surviving rats revealed gradual alleviation of this condition. At 14 weeks post-exposure, there were no further signs of diarrhea.

There were six deaths during the 6 months of exposure. One male monkey died during the seventh week of exposure to RJ-5. Pathology revealed death was due to gastric dilatation of unknown etiology, but believed to be unrelated to exposure. One mouse in each of the exposure groups died from accidental injuries. Remaining mortality was limited to unexposed control rodents. One mouse and one rat died of pneumonia at 1 and 24 weeks, respectively. One rat was necropsied at 10 weeks because of abnormal behavior indicative of middle ear infection.

Mean body weights of exposed monkeys obtained on a biweekly schedule were normal when compared with control weights taken on the same time schedule. However, weight depressions were noted for rats and dogs exposed to RJ-4 and RJ-5.

The growth of rats is shown in Figure 1. Noticeable is the apparently subnormal gain from 2 weeks forward for both exposed groups. The mean weights of the RJ-4 exposed animals are statistically different from control values at all time periods, ranging about 5% lower. Although at several time periods the mean weights of the RJ-5 exposed rats were 10-12 grams less than controls, statistical calculations revealed no significant differences from control weights. The odors of RJ-4 and RJ-5 were very noticeable and objectionable even after purging of the chambers after each exposure period, and this sensory trauma might have caused appetite suppression in rats resulting in growth suppression. To test this theory, food consumption measurements were made over a 3-day period during the 10th week of exposure. The daily results were variable, but overall information suggested there was no real difference in food consumption between control and exposed rats.

Mean body weights of the dog groups are shown in Figure 2. Both exposed groups of dogs gained less weight than controls throughout the course of the study. At first glance, weight depression appears greater for the RJ-5 exposed dogs; however, this is not the case since the RJ-5 group weighed 0.5 kilograms less than the RJ-4 group at the beginning of the study. An examination of initial and final group mean body weights revealed that the controls, the RJ-5, and the RJ-4 groups gained 2.10, 1.22 and 0.98 kilograms, respectively. Therefore, comparable subnormal weight gains occurred for dogs exposed to RJ-4 and RJ-5.

Biweekly clinical blood test results collected on dogs and monkeys showed no abnormalities or trends to adverse hematological effect. The results of these tests are shown in the appendix Tables 1 - 28.

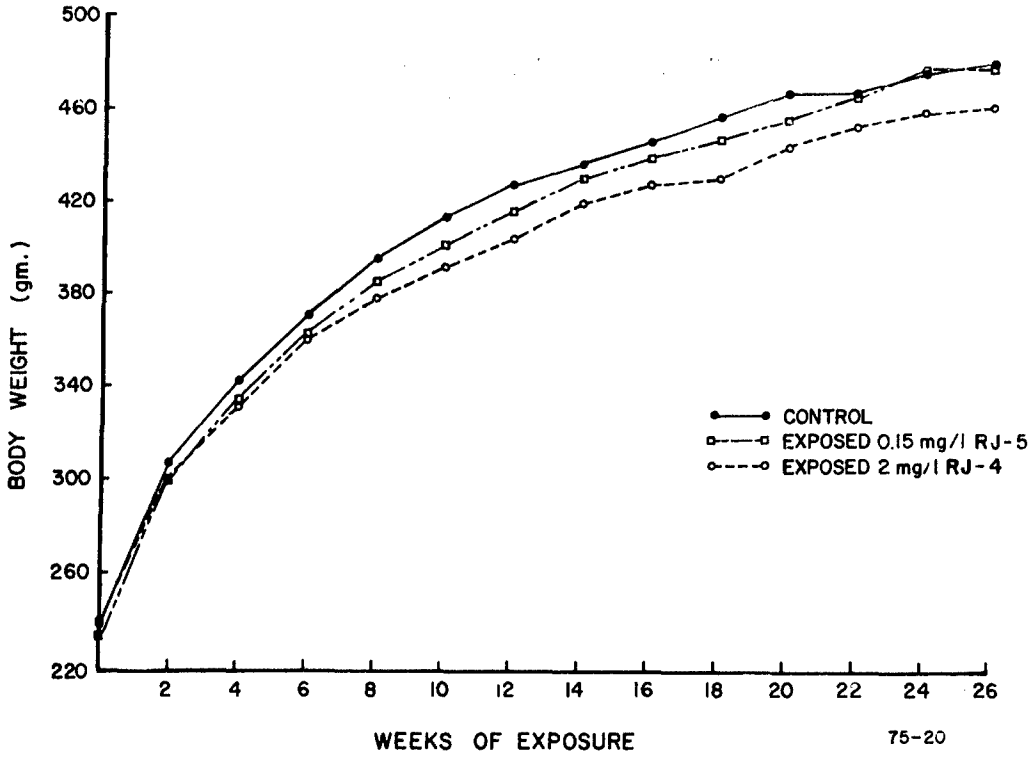

Figure 1. The effect of repeated daily exposures to RJ-4 or RJ-5 on rat growth.

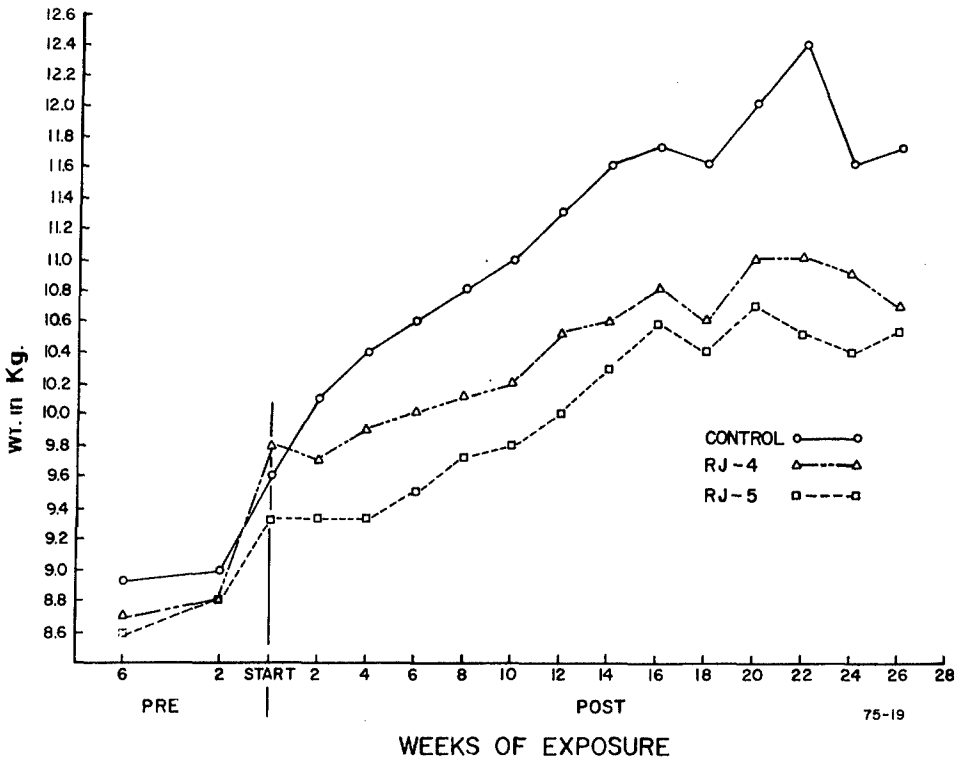

Figure 2. The effect of repeated daily exposures to RJ-4 or RJ-5 on dog growth.

There was no abnormal change in organ weights of rats exposed to RJ-5. Mean organ weights and organ to body weight ratios are shown in Tables 3 and 4, respectively, for rats exposed to RJ-4, RJ-5 and controls. No toxicologic significance is attached to the lung weight difference between RJ-4 or RJ-5 exposed and control rodents in that the body weights of RJ-4 and RJ-5 exposed rodents were also significantly lower than controls. However, mean liver and kidney weights as well as the ratios for the RJ-4 exposed rats are statistically higher than control values.

TABLE 3. THE EFFECT OF 6-MONTH CHRONIC INHALATION EXPOSURE TO RJ-4 AND RJ-5 ON RAT ORGAN WEIGHT

(Mean Weight in Grams)

	Unexposed Controls N=28	Exposed RJ-4 N=20	Exposed RJ-5 N=20
Body Wt.	459	442	453
± S.D.	32	38	45
Heart Wt.	1.6	1.5	1.4
± S.D.	0.2	0.3	0.3
Lung Wt.	2.2	1.9**[2]	1.9**[2]
± S.D.	0.3	0.2	0.2
Liver Wt.	13.0	15.6**[1]	13.3
± S.D.	1.6	2.3	2.5
Spleen Wt.	0.9	0.8	0.9
± S.D.	0.2	0.2	0.3
Kidney Wt.	3.2	3.5**[1]	3.2
± S.D.	0.3	0.4	0.4

**Statistically different from control at 0.01 level.
[1]Significantly higher than control.
[2]Significantly lower than control.

TABLE 4. THE EFFECT OF CHRONIC INHALATION EXPOSURE TO RJ-4 AND RJ-5 ON RAT ORGANS

(Organ/Body Weight Ratios $x10^2$)

	Unexposed Controls N=28	Exposed RJ-4 N=20	Exposed RJ-5 N=20
Heart/Body ± S.D.	0.339 0.04	0.333 0.05	0.314 0.05
Lung/Body ± S.D.	0.471 0.06	0.435*[2] 0.04	0.432*[2] 0.06
Liver/Body ± S.D.	2.820 0.24	3.536**[1] 0.48	2.918 0.34
Spleen/Body ± S.D.	0.198 0.04	0.188 0.03	0.203 0.06
Kidney/Body ± S.D.	0.674	0.792**[1]	0.702

**Statistically different from control at 0.01 level.
[1]Significantly higher than control.
[2]Significantly lower than control.

Gross pathology results for animals sacrificed at exposure conclusion revealed no changes attributed to RJ-4 or RJ-5 exposure. There were no significant histopathology findings in monkeys and mice. However, acute inflammation was noted in the lungs of dogs and rats exposed to RJ-4 and RJ-5. This information is shown in Table 5. Lung lesions were restricted to male RJ-4 and female RJ-5 exposed dogs while 8 of 20 RJ-4 exposed rats and 6 of 20 RJ-5 exposed rats showed bronchopneumonia.

TABLE 5. LUNG HISTOPATHOLOGY IN DOGS AND RATS EXPOSED TO RJ-4 AND RJ-5

	RJ-4 Exposed			RJ-5 Exposed			Controls		
	Dogs		Rats	Dogs		Rats	Dogs		Rats
	♂	♀	♂	♂	♀	♂	♂	♀	♂
Broncho-pneumonia	3/4	0/4	8/20	0/4	2/4	6/20	0/4	0/4	2/20
Bronchitis	1/4	0/4	1/20	0/4	3/4	0/20	0/4	0/4	1/20
Abscess	0/4	0/4	0/20	1/4	0/4	0/20	0/4	0/4	0/20

Cause of death in groups of 20 rats and mice during the 12-month postexposure observation period, almost without exception, was pneumonia. Table 6 shows the number of rodent survivors at sacrifice one year postexposure. Gross pathology results for the

few remaining rats, 2 RJ-5 exposed and 3 controls, revealed chronic respiratory infection in all cases. Nodules, tumor-like lesions, were seen on the lungs of exposed and control mice. One control mouse, 3 RJ-4, and 5 RJ-5 exposed mice showed these lesions.

TABLE 6. JP-9 STUDY SURVIVORS AT ONE YEAR POSTEXPOSURE

Group	Rats	Mice
RJ-4 Exposed	0/20	12/20
RJ-5 Exposed	2/20	14/20
Control	3/20	12/20

Histologic examination of rats that died or were killed during the 52nd week postexposure observation period were remarkably similar, with consistent findings of chronic respiratory disease and glomerulonephrosis. One RJ-5 exposed rat that survived the entire postexposure period had thyroid carcinoma.

Mice that died during the postexposure period had a high incidence of pathologic change in all three groups as shown in Table 7.

TABLE 7. INCIDENCE OF TUMORS IN MICE THAT DIED DURING THE POSTEXPOSURE PERIOD

	Control	RJ-4 Exposed	RJ-5 Exposed
Sarcomas	2/5	3/6	4/6
Alveolargenic Carcinomas	1/5	0/6	0/6
Other Tumors	0/5	1/6	0/6

Most of the sarcomatous lesions observed were undifferentiated but were thought to be of hemopoietic origin. These lesions were commonly seen in multiple organs including the lung, spleen, liver, and kidney. Table 7 shows total incidence of the significant lesions found in all mice during the 52 week postexposure observation period.

No deaths attributable to exposure occurred in four animal species during 6-month inhalation exposures to near saturation concentrations of RJ-4 and RJ-5. Dogs and rats in both exposure groups experienced body weight depressions relative to their controls. Mean liver and kidney weights as well as their ratios were significantly elevated in RJ-4 exposed rats when compared with control data. Histopathology which included Oil-Red-O staining failed to reveal any fat deposition or abnormal alterations in liver and kidney tissue which could account for increased organ

weights in RJ-4 rats. Histopathologic findings in exposed monkeys and mice showed no abnormalities that were treatment related. However, for dogs and rats, the frequencies of pulmonary inflammation including abscesses, bronchopneumonia, and bronchitis, suggest respiratory irritation with the probability of secondary bacterial inflammation. The results of clinical hematology and chemistry tests performed on dogs and monkeys provide evidence that no kidney, liver or hematologic toxicity occurred from chronic exposure to RJ-4 or RJ-5 vapors.

TABLE 7. INCIDENCE OF SIGNIFICANT LESIONS IN MICE EXPOSED TO JP-9 CONSTITUENTS

	Controls	RJ-4 Exposed	RJ-5 Exposed
Lymphosarcoma	0/17	0/18	2/20
Alveolargenic Carcinoma	1/17	0/18	5/20
Alveolargenic Adenoma	0/17	2/18	0/20
Bronchogenic Carcinoma	0/17	0/18	1/20
Hemopoietic Sarcoma	2/17	2/18	3/20
Myelosarcoma	1/17	1/18	1/20
Total Tumors	4/17	5/18	12/20

CONCLUSIONS

The results of this study demonstrate the low order of toxicity of JP-9 constituents exhibited in experimental animals. Kidney and liver hyperplasia in RJ-4 exposed rats and pulmonary irritation in dogs and monkeys exposed to RJ-4 and RJ-5 emerge as the salient results of this study. Although the reasons for organ hyperplasia in rats is not clear, little toxicologic significance is implied since there was no tissue destruction or alteration. Although there is increased tumor incidence in a small number of mice held for one year after exposure to near saturated RJ-5 vapors, there is no clear evidence that this compound is carcinogenic. The finding of respiratory irritation should be considered relative to possible human experience of chronic exposure to RJ-4 or RJ-5. Due to their low vapor pressures, the inhalation hazard (the probability of injury in use) is extremely low. The odors of RJ-4 and RJ-5 are extremely objectionable and it is, therefore, doubtful that workers would tolerate exposures even at concentrations far less than those used in this study for any substantial time period. Furthermore, as the most volatile component of JP-9 fuel is methylcyclohexane, the toxicity of the mixture would be largely that of this compound.

However, considering RJ-4 and RJ-5 as separate entities, RJ-4 shows a relatively low order of toxicity in experimental animals and is judged to be a minor inhalation hazard to man while RJ-5 should be considered a suspect carcinogen until further investigation clarifies this matter.

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APPENDIX
ANIMAL EXPOSURE DATA

APPENDIX TABLE 1. MEAN HEMATOCRIT VALUES[1] OF DOGS[2] EXPOSED TO CONSTITUTENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Control	RJ-4 Exposed	RJ-5 Exposed
-6	43	42	43
-2	44	43	46
0	43	42	44
2	44	43	46
4	46	47	49
6	46	47	49
8	46	46	47
10	46	45	47
12	46	44	45
14	45	44	45
16	46	44	46
18	47	45	47
20	45	45	47
22	44	45	46
24	43	45	46
26	45	45	46

[1]Volume Percent
[2]N = 8

APPENDIX TABLE 2. MEAN HEMOGLOBIN VALUES[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	14.4	13.9	14.6
-2	14.0	13.9	14.9
0	14.4	14.1	14.8
2	14.3	14.3	14.5
4	15.1	15.4	16.0*
6	15.7	15.6	16.3
8	15.1	14.9	15.4
10	15.5	15.3	15.8
12	15.5	14.8	15.2
14	15.3	15.1	15.3
16	16.0	15.1	15.9
18	15.5	15.3	16.8*
20	15.2	15.3	16.1
22	15.0	15.3	15.8
24	14.6	15.0	15.6
26	15.3	15.4	15.8

[1]g%
[2]N = 8
*Statistically different from control at 0.05 level.

APPENDIX TABLE 3. MEAN RED BLOOD CELL COUNTS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	6.3	6.1	6.2
-2	6.3	6.6	6.6
0	6.2	6.1	6.1
2	6.2	6.5	6.6
4	6.3	6.4	6.5
6	6.1	6.3	6.4
8	6.2	6.0	6.3
10	6.5	6.0	6.4
12	5.5	5.4	5.7
14	6.2	6.2	6.3
16	6.1	5.7	6.0
18	5.7	5.2*	5.8
20	6.1	6.1	6.2
22	6.0	6.2	6.3
24	5.9	6.2	6.2
26	6.5	6.3	6.6

[1]Red Blood Cell Count $x10^6$
[2]N = 8
*Statistically different from control at 0.05 level.

APPENDIX TABLE 4. MEAN WHITE BLOOD CELL COUNTS[1] IN DOGS[2] EXPOSED TO CONSTITUTENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	13.0	12.2	11.9
-2	10.9	13.1	13.0
0	10.2	12.2	11.9
2	13.6	12.5	11.1
4	11.7	12.3	13.8
6	10.9	12.2	10.7
8	12.4	13.1	11.7
10	12.4	11.7	10.9
12	12.5	11.6	16.3
14	11.5	11.2	11.1
16	12.0	13.6	10.7
18	19.3	15.7	14.1*
20	11.0	12.2	12.7
22	11.7	12.2	12.8
24	10.9	11.4	12.9
26	10.1	11.2	13.2

[1]White Blood Cell Count $x10^3$
[2]N = 8
*Statistically different from control at 0.05 level.

APPENDIX TABLE 5. MEAN RETICULOCYTE COUNTS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	2.0	2.5	2.6
-2	0.5	1.0	0.9
0	0.5	0.5	0.9
2	0.2	0.3	0.5**
4	0.2	0.3	0.4
6	0.5	0.6	0.7
8	0.3	0.5	0.4
10	0.4	0.5	0.5
12	0.3	0.3	0.3
14	0.5	0.5	0.7
16	0.3	0.6	0.8*
18	0.5	0.4	0.5
20	0.6	0.4	0.6
22	0.7	0.7	0.7
24	0.7	0.7	0.9
26	0.5	0.5	0.6

[1]
[2]No. Reticulocytes/100 RBC
N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 6. MEAN SODIUM LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	146	147	149
-2	148	147	148
0	149	152**	150
2	146	147	149*
4	152	153	151
6	147	149	151*
8	148	148	147
10	150	147**	147**
12	151	149	150
14	150	148	147*
16	147	149	147
18	146	148	146
20	147	147	149
22	148	148	147
24	148	148	147*
26	151	149	149

[1]
[2]mEq/L
N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 7. MEAN POTASSIUM LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	4.7	4.8	4.9
-2	4.7	4.8	4.9
0	4.8	4.9	4.9
2	4.8	4.9	4.9
4	4.9	4.8	4.9
6	4.6	4.8*	4.8
8	4.7	4.6	4.6
10	4.8	4.6**	4.5**
12	4.8	4.6	4.6
14	4.8	4.7	4.7
16	4.7	4.7	4.7
18	4.6	4.5	4.5
20	4.6	4.7	4.6
22	4.7	4.6	4.5*
24	4.4	4.7*	4.3
26	4.6	4.7	4.6

[1]mEq/L
[2]N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 8. MEAN SERUM CALCIUM LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	10.3	10.2	10.1
-2	9.9	9.9	10.1
0	10.0	10.2	10.1
2	9.8	10.0	10.0
4	10.5	10.3	10.5
6	10.1	10.0	10.1
8	10.2	10.2	10.2
10	9.9	9.8	10.0
12	9.8	9.8	10.0
14	9.9	9.9	9.9
16	9.8	9.7	9.6*
18	9.7	9.6	9.7
20	9.5	9.5	9.6
22	9.5	9.6	9.5
24	9.7	9.7	9.6*
26	9.9	9.8	9.6**

[1]mg %
[2]N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 9. MEAN SERUM ALBUMIN LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	3.0	2.9	3.0
-2	3.1	3.0	3.1
0	3.0	2.8*	3.1
2	2.7	3.0*	3.2**
4	3.0	2.7*	3.1
6	2.8	2.7	2.9
8	3.2	3.1	3.2
10	3.1	3.1	3.2
12	2.8	2.9	3.3**
14	2.8	2.1**	2.4*
16	3.0	2.9*	3.3**
18	2.9	3.1	3.2
20	3.0	3.0	3.1
22	3.1	2.9	3.2
24	2.7	2.8	2.9
26	3.0	2.7**	3.2

[1] g%
[2] N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 10. MEAN SERUM GLOBULIN LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	2.9	2.9	2.7
-2	2.7	2.8	3.0
0	2.9	3.1	2.9
2	3.3	3.1	3.0
4	3.1	3.1	3.1
6	3.1	3.4*	3.2
8	3.2	3.3	3.1
10	3.5	3.4	3.3
12	3.2	3.1	3.1
14	3.5	4.1**	3.9*
16	3.3	3.3	3.2
18	3.3	3.4	3.3
20	3.3	3.5	3.3
22	3.2	3.4	3.0
24	3.5	3.6	3.2
26	3.4	3.6	2.9

[1] g%
[2] N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 11. MEAN SERUM TOTAL PROTEIN LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	5.9	5.8	5.7
-2	5.8	5.8	5.9
0	5.8	5.8	5.9
2	6.0	6.2	6.3*
4	6.0	5.8	6.2
6	5.9	6.1*	6.1*
8	6.4	6.3	6.3
10	6.6	6.5	6.5
12	6.0	6.0	6.4*
14	6.2	6.2	6.3
16	6.4	6.1	6.5
18	6.3	6.4	6.4
20	6.3	6.5	6.4
22	6.2	6.3	6.3
24	6.2	6.3	6.2
26	6.4	6.3	6.1

[1] g%
[2] N = 8
*Statistically different from control at 0.05 level.

APPENDIX TABLE 12. MEAN BLOOD GLUCOSE LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	113	120	121
-2	116	116	124
0	113	114	127*
2	108	108	102
4	106	110	102
6	108	99**	86**
8	107	108	108
10	112	101**	102
12	101	103	104
14	114	108	117
16	107	110	117*
18	112	108	120
20	109	105	105
22	110	106	109
24	117	112*	118
26	115	111*	114

[1] mg %
[2] N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 13. MEAN SERUM ALKALINE PHOSPHATASE LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	12.6	11.1	16.1
-2	4.4	4.3	5.9
0	5.8	5.3	7.1
2	5.4	5.9	6.7
4	5.1	6.4	6.4
6	5.2	6.4	6.2
8	5.1	6.8	6.1
10	4.3	5.7	5.5
12	5.0	5.9	6.3
14	4.3	5.5	5.3
16	4.3	5.9*	5.6
18	3.6	5.0	4.5
20	4.5	4.6	4.0
22	3.3	4.3	4.7**
24	3.2	4.2	3.4
26	3.2	4.8*	4.4*

[1]King-Armstrong Units
[2]N = 8
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 14. MEAN SERUM GLUTAMIC PYRUVIC TRANSAMINASE (SGPT) LEVELS[1] IN DOGS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	18	19	20
-2	27	24	25
0	25	28	23
2	21	26*	23
4	30	30	25
6	29	30	29
8	32	40	35
10	35	32	31
12	41	44	34*
14	38	36	33
16	27	27	24
18	33	33	31
20	34	35	32
22	38	36	34
24	31	33	30
26	33	32	33

[1]Reitman-Frankel Units
[2]N = 8
*Statistically different from control at 0.05 level.

APPENDIX TABLE 15. MEAN HEMATOCRIT VALUES[1] OF MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	41	40	42
-2	40	42	41
0	39	41	43
2	39	38	43*
4	39	39	42
6	39	41	42
8	40	39	42
10	39	39	43*
12	39	39	41
14	40	39	42
16	39	38	40
18	41	39	41
20	40	39*	41
22	39	38	40
24	39	40	42
26	39	39	41

[1]Volume Percent
[2]N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 16. MEAN HEMOGLOBIN LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	12.8	13.0	13.4
-2	13.0	13.1	13.8
0	12.4	12.8	13.7
2	12.4	12.0	13.0
4	12.3	12.3	13.2
6	12.4	12.8	13.1
8	12.5	12.4	13.2
10	12.5	12.8	13.6*
12	11.8	12.2	13.1
14	12.7	12.9	14.0
16	12.7	12.3	13.0
18	12.9	12.7	13.4
20	12.6	12.4	13.4
22	12.7	12.3	13.0
24	12.4	12.4	13.0
26	12.7	12.7	13.2

[1]g%
[2]N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 17. MEAN RED BLOOD CELL COUNTS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	5.5	5.6	5.9
-2	5.4	5.7	5.9*
0	5.3	5.7	6.0*
2	5.0	5.0	5.9**
4	5.1	5.3	5.4
6	5.1	5.3	5.4
8	5.2	5.1	5.1
10	5.0	5.1	5.4*
12	4.5	4.6	4.8
14	5.1	5.5	5.7*
16	5.2	5.9	5.1
18	5.2	5.2	6.0*
20	5.3	5.2	5.3
22	5.0	5.2	5.5
24	5.0	5.1	5.6
26	5.1	5.8	5.4

[1]Red Blood Cell Count $x10^6$
[2]N = 4
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 18. MEAN WHITE BLOOD CELL COUNTS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	12.1	9.3	10.5
-2	10.4	9.3	10.1
0	10.8	9.7	8.7
2	10.4	13.2	11.3
4	14.9	11.1	9.7*
6	8.9	8.3	9.4
8	9.3	9.7	9.6
10	12.7	9.8	10.6
12	9.6	8.7	10.0
14	8.7	9.7	10.7
16	11.0	13.4	13.0
18	8.8	16.4	11.9
20	9.8	9.4	9.8
22	10.0	10.0	9.7
24	9.4	10.3	11.2
26	9.9	10.3	9.7

[1]White Blood Cell Count $x10^3$
[2]N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 19. MEAN RETICULOCYTE COUNTS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	1.4	0.9	1.2
-2	0.8	0.9	0.8
0	0.8	0.9	0.8
2	0.3	0.2	0.4
4	0.2	0.2	0.4
6	0.2	0.3	0.2
8	0.5	0.3	0.2
10	0.2	0.3	0.3
12	0.3	0.1	0.1
14	0.3	0.7	0.5
16	0.6	0.5	1.0
18	0.8	0.5	0.6
20	0.5	0.6	0.5
22	1.0	0.8	1.0
24	0.8	1.2	0.6
26	0.8	0.7	0.7

[1]No. Reticulocytes/100 RBC
[2]N = 4

APPENDIX TABLE 20. MEAN SODIUM LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	149	149	150
-2	148	153	152
0	148	149	151
2	150	151	149
4	151	152	149
6	151	152	153
8	149	150	150
10	146	149*	149
12	152	152	152
14	153	151	148
16	151	150	152
18	151	149	148
20	149	147	154
22	147	148	146
24	150	148*	149
26	149	154	150

[1]mEq/L
[2]N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 21. MEAN POTASSIUM LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	3.6	3.7	3.9
-2	3.9	4.6	4.0
0	4.1	4.3	4.3
2	4.6	5.0	4.7
4	4.9	4.7	4.4
6	4.4	5.0**	5.9
8	4.7	4.5	4.4
10	4.6	5.0	4.3
12	4.8	4.6	4.4
14	4.4	4.9	4.3
16	5.2	4.9	4.8
18	4.6	4.9	4.1
20	4.7	4.4	4.5
22	4.5	4.6	4.6
24	4.4	4.3	4.4
26	4.0	4.6	4.6

[1]mEq/L
[2]N = 4
**Statistically different from control at 0.01 level.

APPENDIX TABLE 22. MEAN SERUM CALCIUM LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	10.2	10.2	10.3
-2	10.3	10.7	10.6
0	10.1	10.2	10.3
2	10.3	10.5	10.2
4	11.5	10.7	10.6*
6	10.9	11.1	10.6
8	10.4	10.6	10.3
10	10.0	10.3	10.3
12	10.5	10.3	10.7
14	10.6	10.3	10.0*
16	10.6	10.5	10.6
18	10.3	10.4	10.2
20	10.2	10.0	10.6
22	10.1	10.2	10.3
24	10.1	10.1	10.1
26	10.1	10.1	9.7*

[1]mg %
[2]N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 23. MEAN SERUM ALBUMIN LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	4.1	4.3	4.3
-2	4.9	5.1	5.1
0	4.4	4.5	4.7
2	4.6	4.1*	4.4
4	4.0	4.0	4.2
6	4.1	3.6*	4.3
8	4.6	4.5	4.7
10	5.0	4.5	4.5
12	4.0	4.0	4.6
14	3.6	3.9	3.8
16	4.1	4.1	4.5
18	4.2	4.3	4.8**
20	4.3	4.3	4.6*
22	4.3	4.3	4.6
24	4.0	4.1	3.8
26	4.3	4.1	4.3

[1] g%
[2] N = 4
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

APPENDIX TABLE 24. MEAN SERUM GLOBULIN LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	3.7	3.6	3.7
-2	4.0	3.8	3.5
0	3.3	3.2	3.2
2	3.3	3.8*	3.5
4	4.0	3.9	3.5
6	3.4	4.0*	3.0
8	3.4	3.4	2.9
10	3.0	3.5	3.4
12	3.6	3.4	3.2
14	3.9	4.0	3.8
16	3.6	3.4	3.1
18	3.3	3.5	2.8
20	2.9	3.3	3.3
22	3.0	3.3	2.8
24	3.2	3.5	3.7
26	3.3	3.7	2.8

[1] g%
[2] N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 25. MEAN SERUM TOTAL PROTEIN LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	7.7	7.9	7.9
-2	8.9	8.8	8.6
0	7.6	7.7	7.9
2	7.9	7.8	7.9
4	8.0	8.0	7.7
6	7.5	7.6	7.4
8	8.0	7.8	7.7
10	8.0	8.0	7.8
12	7.6	7.4	7.7
14	7.4	7.8	7.5
16	7.7	7.5	7.6
18	7.5	7.8	7.5
20	7.2	7.5	7.9*
22	7.3	7.6	7.5
24	7.2	7.6	7.5
26	7.5	7.7	7.1

[1] g%
[2] N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 26. MEAN BLOOD GLUCOSE LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	99	115	123
-2	90	105	102
0	96	118	114*
2	120	105	118
4	89	93	117
6	88	93	155
8	103	106	108
10	108	94	89
12	89	86	98
14	95	100	142*
16	89	93	98
18	97	105	99
20	89	99	92
22	87	97	101
24	84	106*	103*
26	87	114*	103

[1] mg %
[2] N = 4
*Statistically different from control at 0.05 level.

APPENDIX TABLE 27. MEAN SERUM ALKALINE PHOSPHATASE LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	103	100	76
-2	94	95	74
0	45	52	48
2	47	44	43
4	45	49	48
6	50	47	48
8	47	38	40
10	48	36	38
12	49	45	48
14	43	40	40
16	45	42	50
18	48	37	38
20	45	38	38
22	41	38	41
24	42	36	36
26	53	40	37

[1]King-Armstrong Units
[2]N = 4

APPENDIX TABLE 28. MEAN SERUM GLUTAMIC PYRUVIC TRANSAMINASE (SGPT) LEVELS[1] IN MONKEYS[2] EXPOSED TO CONSTITUENTS OF JP-9 AND THEIR UNEXPOSED CONTROLS

Exposure Weeks	Unexposed Controls	RJ-4 Exposed	RJ-5 Exposed
-6	22	31	37
-2	23	20	30
0	40	38	54
2	24	23	41
4	25	24	34
6	34	31*	46
8	37	33	41
10	31	31	35
12	40	38	47
14	46	31*	38
16	32	25	27
18	38	29	43
20	35	30	38
22	39	33*	39
24	33	30	33
26	40	28**	30*

[1]Reitman-Frankel Units
[2]N = 4
*Statistically different from control at 0.05 level.
**Statistically different from control at 0.01 level.

*U.S.Government Printing Office: 1978 — 757-080/622